

Exhibit E

MARSTELLER & ASSOCIATES

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Attorneys and Counselors
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Thomas F. Marsteller, Esq.
Email: TMarsteller@MarstellerLaw.com

Patents, Trademarks
& Copyrights

December 5, 2008

FACSIMILE TRANSMITTAL SHEET

TO: PCT/DO/EO (571) 273-3201
FROM: T.F. MARSTELLER LUZ033PU
Client / Matter Number

RE: RESPONSE TO NOTICE TO FILE MISSING
REQUIREMENTS UNDER 35 U.S.C. 371 IN THE DO/EO/US

In re Application of: Raphael Meehoulam; Natalya M. Kogan; Ruth Rabinowitz;
and, Michael Schlesinger

Serial No.: 10/597,166
Confirmation No.: 7062
PCT No.: PCT/IL2005/000053
Filed: January 14, 2005

For: THERAPEUTIC USE OF QUINONOID DERIVATIVES OF
CANNABINOIDS

NUMBER OF COPIES, INCLUDING THIS TRANSMITTAL SHEET:

Legal: _____
Letter: 32 SEE COMMENTS BELOW

SHOULD YOU HAVE ANY PROBLEM RECEIVING OUR TRANSMISSION, PLEASE
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TIME SENT:

****COMMENT**:** NO CONFIRMATION.

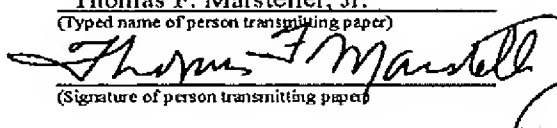
/LUZ033PU/FAX PTO 120508.DOC

CERTIFICATE OF TRANSMISSION (37 CFR 1.8(a))

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being facsimile transmitted on the date shown below to the Patent and Trademark Office (Fax No. (571) 273-3201).

Date: December 5, 2008

Thomas F. Marsteller, Jr.
(Typed name of person transmitting paper)

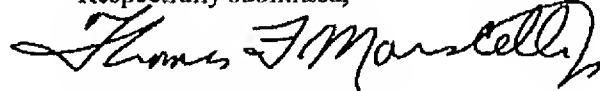

(Signature of person transmitting paper)

\\LUZ033PUCERT TRANSMISSION 120508.DOC.DOCX

Applicants further submit herewith:

1. A copy of the Notice to File Missing Requirements under 35 U.S.C. 371 in the United States Designated/Elected Office (DO/EO/US).
2. A new Declaration (Form PTO/SB/01) executed by the inventors.
3. A credit card authorization in the amount of \$745.00 is submitted with the filing of this paper for the payment of the total additional fees required for this application as a small entity in accordance with the statement in the Notice.
4. A Preliminary Amendment reasserting the claims originally electronically filed with the subject national stage application.
5. A Certificate of Transmission by facsimile for the accompanying documents.

Respectfully submitted,



Thomas F. Marsteller, Jr.
Registration No. 29,672

Marsteller & Associates, P.C.
PO Box 803302
Dallas, TX 75380-3302
(972) 233-0939
(972) 386-3907 (Fax)

Date: December 4, 2008



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 142
Alexandria, Virginia 22304-1120
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| | | |
|--|--|------------------------------|
| U.S. APPLICATION NUMBER NO. 10/597,166 22948 MARSTELLER & ASSOCIATES P O BOX 803302 DALLAS, TX 75380-3302 | FIRST NAMED APPLICANT Raphael Mechoulam | ATTY. DOCKET NO. LUZ033PU |
| INTERNATIONAL APPLICATION NO. PCT/IL2005/000053 | | |
| LA. FILING DATE 01/14/2005 | | PRIORITY DATE 01/15/2004 |

CONFIRMATION NO. 7062
371 FORMALITIES LETTER



Date Mailed: 07/21/2008

**NOTIFICATION OF MISSING REQUIREMENTS UNDER 35 U.S.C. 371
IN THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US)**

The following items have been submitted by the applicant or the IB to the United States Patent and Trademark Office as an Elected Office (37 CFR 1.495):

- Indication of Small Entity Status
- Priority Document
- Copy of the International Application filed on 07/13/2006
- Copy of the International Search Report filed on 07/13/2006
- Copy of IPE Report filed on 07/13/2006
- Oath or Declaration filed on 07/13/2006
- U.S. Basic National Fees filed on 07/13/2006
- Priority Documents filed on 07/13/2006
- Power of Attorney filed on 07/13/2006
- Specification filed on 07/13/2006
- Claims filed on 07/13/2006
- Abstracts filed on 07/13/2006
- Drawings filed on 07/13/2006

The applicant needs to satisfy supplemental fees problems indicated below.

The following items **MUST** be furnished within the period set forth below in order to complete the requirements for acceptance under 35 U.S.C. 371:

- Additional claim fees of \$745 as a small entity, including any required multiple dependent claim fee, are required. Applicant must submit the additional claim fees or cancel the additional claims for which fees are due.
- Oath or declaration of the Inventors, in compliance with 37 CFR 1.497(a) and (b), identifying the application by the International application number and international filing date. The current oath or declaration does not comply with 37 CFR 1.497(a) and (b) in that it:
 - Applicant submitted what appears to be two different declarations. While each inventor need not execute the same oath or declaration, each oath or declaration executed by an inventor must contain a complete listing of all inventors so as to clearly indicate what each inventor believes to be the appropriate inventive entity. There is no indication whether the inventors are aware that any other inventor was claimed on the above-captioned application except as listed on the page they signed.

12/09/2008 MKAYPAGH 00000013 10597166

01 FC:2615 350.00 OP
02 FC:2614 210.00 OP
03 FC:2616 105.00 OP

FORM PCT/DO/EO/905 (371 Formalities Letter)

page 1 of 3

SUMMARY OF FEES DUE:

Total additional fees required for this application is \$745 for a Small Entity:

- This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 CFR 1.821(c). Applicant must provide an initial paper or compact disc copy of the "Sequence Listing", as well as an amendment specifically directing its entry into the application and a statement that the content of the sequence listing information recorded in computer readable form is identical to the written (on paper or compact disc) sequence listing and, where applicable, includes no new matter, as required by 37 CFR 1.821(e), 1.821(f), 1.821(g), 1.825(b), or 1.825(d). If the effective filing date is on or after September 8, 2000, see the final rulemaking notice published in the Federal Register at 65 FR 54604 (September 8, 2000) and 1238 OG 145 (September 19, 2000).
- A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 CFR 1.821(e). If the effective filing date is on or after September 8, 2000, see the final rulemaking notice published in the Federal Register at 65 FR 54604 (September 8, 2000) and 1238 OG 145 (September 19, 2000). Applicant must provide an initial computer readable form (CRF) copy of the "Sequence Listing" and a statement that the content of the sequence listing information recorded in computer readable form is identical to the written (on paper or compact disc) sequence listing and, where applicable, includes no new matter, as required by 37 CFR 1.821(e), 1.821(f), 1.821(g), 1.825(b), or 1.825(d). If applicant desires the sequence listing in the instant application to be identical with that of another application on file in the U.S. Patent and Trademark Office, such request in accordance with 37 CFR 1.821(e) may be submitted in lieu of a new CRF.

Total additional claim fee(s) for this application is \$745

- \$210 for 4 independent claims over 3.
- \$350 for 35 total claims over 20.
- \$185 for multiple dependent claim surcharge.

Applicant is cautioned that correction of the above items may cause the specification and drawings page count to exceed 100 pages. If the specification and drawings exceed 100 pages, applicant will need to submit the required application size fee.

For questions regarding compliance to 37 CFR 1.821-1.825 requirements, please contact:

- For Rules Interpretation, call (571) 272-0951
- For PatentIn Software Program Help, call Patent EBC at 1-866-217-9197 or directly at 703-305-3028 / 703-308-6845 between the hours of 6 a.m. and 12 midnight, Monday through Friday, EST.
- Send e-mail correspondence for PatentIn Software Program Help @ ebc@uspto.gov

ALL OF THE ITEMS SET FORTH ABOVE MUST BE SUBMITTED WITHIN TWO (2) MONTHS FROM THE DATE OF THIS NOTICE OR BY 32 MONTHS FROM THE PRIORITY DATE FOR THE APPLICATION, WHICHEVER IS LATER. FAILURE TO PROPERLY RESPOND WILL RESULT IN ABANDONMENT.

The time period set above may be extended by filing a petition and fee for extension of time under the provisions of 37 CFR 1.136(a).

Applicant is reminded that any communications to the United States Patent and Trademark Office must be mailed to the address given in the heading and include the U.S. application no. shown above (37 CFR 1.5)

Registered users of EFS-Web may alternatively submit their reply to this notice via EFS-Web.
<https://portal.uspto.gov/authenticate/AuthenticateUserLocalEPE.html>

For more information about EFS-Web please call the USPTO Electronic Business Center at 1-866-217-9197 or visit our website at <http://www.uspto.gov/ebc>.

If you are not using EFS-Web to submit your reply, you must include a copy of this notice.

BARBARA A CAMPBELL

Telephone: (703) 308-9140 EXT 217

page 3 of 3

FORM PCT/DO/EO/905 (3/11 Formalities Notice)

Doc Code: OATH

Document Description: Oath or declaration filed

PTO/SB/61 (10-09)
 Approved for use through 06/30/2010, OMB 0551-C032
 U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE
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| | | | |
|---|--|------------------------|-------------------|
| DECLARATION FOR UTILITY OR DESIGN PATENT APPLICATION (37 CFR 1.63) | | Attorney Docket Number | LUZ033PU |
| | | First Named Inventor | Raphael Mechoulam |
| <input type="checkbox"/> Declaration Submitted With Initial Filing OR <input checked="" type="checkbox"/> Declaration Submitted after Initial Filing (surcharge (37 CFR 1.16 (f)) required) | | COMPLETE IF KNOWN | |
| | | Application Number | 10597166 |
| | | Filing Date | 07/13/08 |
| | | Art Unit | |
| | | Examiner Name | |

I hereby declare that: (1) Each inventor's residence, mailing address, and citizenship are as stated below next to their name; and (2) I believe the inventor(s) named below to be the original and first inventor(s) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

THERAPEUTIC USE OF QUINONOID DERIVATIVES OF CANNABINOID

(Title of the invention)

the application of which

☐ Is attached hereto
 OR

☒ was filed on (MM/DD/YYYY) 07/13/2008 as United States Application Number or PCT International

Application Number 10597166 and was amended on (MM/DD/YYYY) (if applicable).

I hereby state that I have reviewed and understand the contents of the above identified application, including the claims, as amended by any amendment specifically referred to above.

I acknowledge the duty to disclose information which is material to patentability as defined in 37 CFR 1.56, including for continuation-in-part applications, material information which became available between the filing date of the prior application and the national or PCT International filing date of the continuation-in-part application.

Authorization To Permit Access To Application by Participating Offices

☐ If checked, the undersigned hereby grants the USPTO authority to provide the European Patent Office (EPO), the Japan Patent Office (JPO), the Korean Intellectual Property Office (KIPO), and any other intellectual property offices in which a foreign application claiming priority to the above-identified application is filed access to the above-identified patent application. See 37 CFR 1.14(c) and (h). This box should not be checked if the applicant does not wish the EPO, JPO, KIPO, or other intellectual property office in which a foreign application claiming priority to the above-identified application is filed to have access to the application.

In accordance with 37 CFR 1.14(h)(3), access will be provided to a copy of the application-as-filed with respect to: 1) the above-identified application, 2) any foreign application to which the above-identified application claims priority under 35 USC 119(a)-(d) if a copy of the foreign application that satisfies the certified copy requirement of 37 CFR 1.55 has been filed in the above-identified US application, and 3) any U.S. application from which benefit is sought in the above-identified application.

In accordance with 37 CFR 1.14(e), access may be provided to information concerning the date of filing the Authorization to Permit Access to Application by Participating Offices.

(Page 1 of 3)

This collection of information is required by 35 U.S.C. 115 and 37 CFR 1.53. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 21 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.
 If you need assistance in completing this form, call 1-800-PTO-0189 and select option 2.

PTO/SB/01 (10-08)

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U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

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DECLARATION — Utility or Design Patent Application**Claim of Foreign Priority Benefits**

I hereby claim foreign priority benefits under 35 U.S.C. 119(a)-(d) or (f), or 365(b) of any foreign application(s) for patent, inventor's or plant breeder's rights certificate(s), or 365(a) of any PCT international application which designated at least one country other than the United States of America, listed below and have also identified below, by checking the box, any foreign application for patent, inventor's or plant breeder's rights certificate(s), or any PCT international application having a filing date before that of the application on which priority is claimed.

| Prior Foreign Application Number(s) | Country | Foreign Filing Date (MM/DD/YYYY) | Priority Not Claimed | Certified Copy Attached? | |
|-------------------------------------|---------|----------------------------------|--------------------------|--------------------------|-------------------------------------|
| | | | | YES | NO |
| PCT/IL2005/000053 159892 | WO | 01/14/2005 | <input type="checkbox"/> | <input type="checkbox"/> | <input checked="" type="checkbox"/> |
| | IL | 01/15/2004 | <input type="checkbox"/> | <input type="checkbox"/> | <input checked="" type="checkbox"/> |
| | | | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| | | | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |

☐ Additional foreign application numbers are listed on a supplemental priority data sheet PTO/SB/02B attached hereto.

(Page 2 of 3)

PTO/CB-01 (10-05)
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DECLARATION — Utility or Design Patent Application

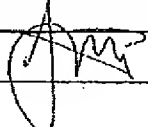

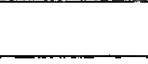
| | | | | |
|--|--|---|-------------|---|
| Direct all correspondence to: | <input checked="" type="checkbox"/> The address associated with Customer Number: | 22945 | OR | <input type="checkbox"/> Correspondence address below |
| Name | | | | |
| Address | | | | |
| City | | State | | ZIP |
| Country | Telephone | | Email | |
| <p>WARNING:</p> <p>Petitioner/applicant is cautioned to avoid submitting personal information in documents filed in a patent application that may contribute to identify them. Personal information such as social security numbers, bank account numbers, or credit card numbers (other than a check or credit card authorization form PTO-2038 submitted for payment purposes) is never required by the USPTO to support a petition or an application. If this type of personal information is included in documents submitted to the USPTO, petitioners/applicants should consider redacting such personal information from the documents before submitting them to the USPTO. Petitioner/applicant is advised that the record of a patent application is available to the public after publication of the application (unless a non-publication request in compliance with 37 CFR 1.213(a) is made in the application) or issuance of a patent. Furthermore, the record from an abandoned application may also be available to the public if the application is referenced in a published application or an issued patent (see 37 CFR 1.14). Checks and credit card authorization forms PTO-2038 submitted for payment purposes are not retained in the application file and therefore are not publicly available. Petitioner/applicant is advised that documents which form the record of a patent application (such as the PTO/SB-01) are placed into the Privacy Act system of records DEPARTMENT OF COMMERCE, COMMERCE-PAT-7. System name: Patent Application Files. Documents not retained in an application file (such as the PTO-2038) are placed into the Privacy Act system of COMMERCE-PAT-11A-10. System name: Deposit Accounts and Electronic Funds Transfer Profiles.</p> <p>I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. 1001 and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.</p> | | | | |
| NAME OF SOLE OR FIRST INVENTOR: | | <input type="checkbox"/> A petition has been filed for this unsigned inventor | | |
| Given Name (first and middle (if any)) | | Family Name or Surname | | |
| Raphael | | MECHOULAM | | |
| Inventor's Signature <i>R. Mechoulam</i> | | | | Date |
| | | | | 26 Nov 08 |
| Residence, City | State | Country | Citizenship | |
| Jerusalem | | Israel | Israel | |
| Mailing Address | | | | |
| 2 Tchernichovsky Street | | | | |
| City | State | Zip | Country | |
| Jerusalem | | 92581 | Israel | |
| <input checked="" type="checkbox"/> Additional inventors or legal representatives are being named on the 1 supplement(s) (change PTO/CB-02A or 02LB attached form). | | | | |

(Page 3 of 3)

PTO/SB/02A (07-07)
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| | |
|--------------------|---|
| DECLARATION | ADDITIONAL INVENTOR(S) Supplemental Sheet |
| Page 1 of 1 | |

| | | | |
|---|-------|---|-------------|
| Name of Additional Joint Inventor, if any: | | <input type="checkbox"/> A petition has been filed for this unsigned inventor | |
| Given Name (first and middle (if any)) | | Family Name or Surname | |
| Naftaly M. | | KOGAN | |
| Inventor's Signature | | Date | |
|  | | 24 Nov 08 | |
| Jerusalem | State | Israel | Israel |
| Residence: City | | Country | Citizenship |
| 63/22 Slon Street, Kiryat HaYovel | | | |
| Mailing Address | | | |
| Jerusalem | State | 66750 | Israel |
| City | | Zip | Country |
| Name of Additional Joint Inventor, if any: | | <input type="checkbox"/> A petition has been filed for this unsigned inventor | |
| Given Name (first and middle (if any)) | | Family Name or Surname | |
| Ruth | | RABINOWITZ | |
| Inventor's Signature | | Date | |
|  | | | |
| Jerusalem | State | Israel | Israel |
| Residence: City | | Country | Citizenship |
| 68/11 Shephar Street, Givat Mordechai | | | |
| Mailing Address | | | |
| Jerusalem | State | 63720 | Israel |
| City | | Zip | Country |
| Name of Additional Joint Inventor, if any: | | <input type="checkbox"/> A petition has been filed for this unsigned inventor | |
| Given Name (first and middle (if any)) | | Family Name or Surname | |
| Michael | | SCHLESINGER | |
| Inventor's Signature | | Date | |
|  | | | |
| Jerusalem | State | Israel | Israel |
| Residence: City | | Country | Citizenship |
| 10A Rabbi Akiva Street | | | |
| Mailing Address | | | |
| Jerusalem | State | 94582 | Israel |
| City | | Zip | Country |

This collection of information is required by 35 U.S.C. 115 and 37 CFR 1.63. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 21 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

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U.S. Patent and Trademark Office, U.S. DEPARTMENT OF COMMERCE

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| | |
|--------------------|---|
| DECLARATION | ADDITIONAL INVENTOR(S) Supplemental Sheet |
| Page 1 of 1 | |

| | | | |
|---|-------|---|-----------------------|
| Name of Additional Joint Inventor, if any: | | <input type="checkbox"/> A petition has been filed for this unsigned inventor | |
| Given Name (first and middle (if any)) | | Family Name or Surname | |
| Natalya M. | | KOGAN | |
| Inventor's Signature | | Date | |
| Jerusalem Residence: City | State | Israel Country | Israel Citizenship |
| 63/22 Stern Street, Kinyot HaYovel | | | |
| Mailing Address | | | |
| Jerusalem City | State | 98760 Zip | Israel Country |
| Name of Additional Joint Inventor, if any: | | <input type="checkbox"/> A petition has been filed for this unsigned inventor | |
| Given Name (first and middle (if any)) | | Family Name or Surname | |
| Ruth | | RABINOWITZ | |
| Inventor's Signature <i>Ruth Rabinowitz</i> | | Date <i>Nov. 30, 2008</i> | |
| Jerusalem Residence: City | State | Israel Country | Israel Citizenship |
| 68/11 Shahar Street, Givat Mordechai | | | |
| Mailing Address | | | |
| Jerusalem City | State | 93720 Zip | Israel Country |
| Name of Additional Joint Inventor, if any: | | <input type="checkbox"/> A petition has been filed for this unsigned inventor | |
| Given Name (first and middle (if any)) | | Family Name or Surname | |
| Michael | | SCHLESINGER | |
| Inventor's Signature <i>Michael Schlesinger</i> | | Date <i>Nov 30, 2008</i> | |
| Jerusalem Residence: City | State | Israel Country | Israel Citizenship |
| 16A Rabbi Akiva Street | | | |
| Mailing Address | | | |
| Jerusalem City | State | 94582 Zip | Israel Country |

This collection of information is required by 35 U.S.C. 115 and 37 CFR 1.63. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 21 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

| | | |
|-------------------------------|---|-----------------|
| In re Application of: | § | |
| Raphael Mechoulam; Natalya M. | § | |
| Kogan; Ruth Rabinowitz; and, | § | |
| Michael Schlesinger | § | Group Art Unit: |
| | § | |
| Serial No.: 10/597166 | § | |
| | § | |
| Confirmation No.: 7062 | § | |
| | § | |
| Filed: July 13, 2006 | § | |
| | § | |
| For: THERAPEUTIC USE OF | § | |
| QUINONOID DERIVATIVES OF | § | |
| CANNABINOIDS | § | |

Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-1450

Sir:

PRELIMINARY AMENDMENT

Please amend the above-identified application as follows:

AMENDMENTS TO THE CLAIMS are reflected in the listing of claims that begins on page 4 of this paper.

REMARKS/ARGUMENTS begin on page 3 of this paper.

Amendments to the Claims:

A version of the claims with markings to show changes is attached as Attachment A. Amended, canceled, and new claims are so indicated in Attachment A. The attached listing of claims will replace all prior versions, and listings, of claims in the application.

REMARKS

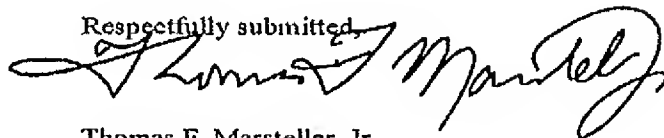
Applicants respectfully request consideration of the instant application on the basis of the amended, canceled and new Claims 1-52.

Conclusion

In light of the amendments and remarks set forth above, Applicants respectfully requests consideration and allowance of Claims 1-52.

If there are matters which can be discussed by telephone to further the prosecution of this Application, Applicants invite the Examiner to call the attorney at the number listed below at the Examiner's convenience.

Respectfully submitted,



Thomas F. Marsteller, Jr.
Registration No. 29,672

Marsteller & Associates, P.C.
PO Box 803302
Dallas, TX 75380-3302
(972) 233-0939
(972) 386-3907 (Fax)

Date: December 4, 2008

LUZ033PU/PRELIMINARY AMENDMENT 120408.DOC

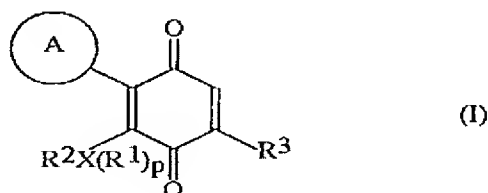
ATTACHMENT A

**LISTING OF CLAIMS WITH MARKINGS
TO SHOW CHANGES MADE**

Attachment A
Listing with Markings
4

Claims:

1. (Original) A pharmaceutical composition comprising as active agent a cannabinoic quinone or an enantiomer thereof, wherein said cannabinoic quinone is a compound of the general formula (I):



wherein,

ring A is 5-, 6-, or 7-membered alicyclic or aromatic ring optionally substituted with from 1 to 3 substituents independently selected from optionally branched C₁-C₆ alkyl, optionally branched C₁-C₆ alkenyl, hydroxy, alkoxy, halo (fluoro, chloro, bromo, iodo), thio, amino and cyano;

X is an oxygen, nitrogen or sulfur atom;

p is zero when X is oxygen or sulfur, or p is 1 when X is nitrogen;

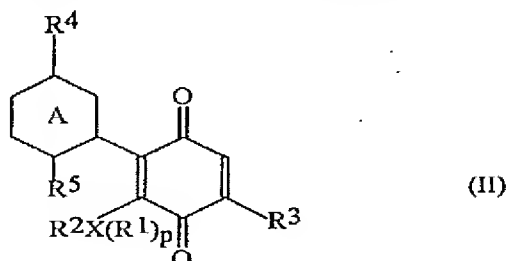
R¹ is H or C₁-C₆ alkyl;

R² designates a substituent selected from H and C₁-C₆ alkyl, or R² designates an optionally branched C₁-C₆ alkylene connected to ring A forming a 6-membered heterocyclic ring comprising atom X, two carbon atoms of the quinone ring to which X is attached and carbon atoms 3 and 4 of ring A;

R³ is optionally branched C₁-C₁₀ alkyl or optionally branched C₁-C₁₀ alkenyl, wherein said alkyl or alkenyl are optionally substituted with hydroxyl, alkoxy, halo (fluoro, chloro, bromo, iodo), thio, amino or cyano;

and optionally further comprising at least one pharmaceutically acceptable additive, diluent and/or carrier.

2. (Original) The pharmaceutical composition of claim 1, wherein said cannabinoic quinone is the compound of formula (II):



wherein

ring A is a cyclohexane, cyclohexene or benzene ring;

X is an oxygen, nitrogen or sulfur atom;

p is zero when X is oxygen or sulfur, or p is 1 when X is nitrogen;

R¹ is H or C₁-C₆ alkyl;

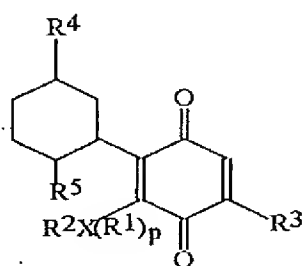
R² designates a substituent selected from H and C₁-C₆ alkyl, or R² designates an optionally branched C₁-C₆ alkylene connected to ring A forming a 6-membered heterocyclic ring comprising atom X, two carbon atoms of the quinone ring to which X is attached and carbon atoms 3 and 4 of ring A;

R³ is optionally branched C₁-C₁₀ alkyl or optionally branched C₁-C₁₀ alkenyl, wherein said alkyl or alkenyl are optionally substituted with hydroxyl, alkoxy, halo (fluoro, chloro, bromo, iodo), thio, amino or cyano;

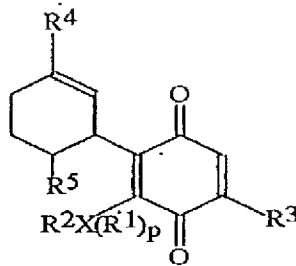
R⁴ is optionally branched C₁-C₆ alkyl or optionally branched C₁-C₆ alkenyl, optionally substituted with hydroxyl, halo (fluoro, chloro, bromo, iodo) thio, amino and cyano; and

R⁵ is optionally branched C₁-C₆ alkyl or optionally branched C₁-C₆ alkenyl, or R⁵ is hydrogen when R² is alkylene.

3. (Currently Amended) The pharmaceutical composition of ~~any one of claims claim 1 and 2~~, wherein said cannabinoic quinone is a compound of one of formulae (III) or (IV), wherein formulae (III) and (IV) have the structure:



(III)



(IV)

wherein

X is an oxygen, nitrogen or sulfur atom;

p is zero when X is oxygen or sulfur, or p is 1 when X is nitrogen;

R¹ is H or C₁-C₆ alkyl;

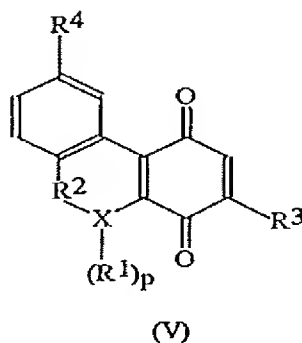
R² designates a substituent selected from H and C₁-C₆ alkyl;

R³ is optionally branched C₁-C₁₀ alkyl or optionally branched C₁-C₁₀ alkenyl, wherein said alkyl or alkenyl are optionally substituted with hydroxyl, alkoxy, halo (fluoro, chloro, bromo, iodo), thio, amino or cyano; and

R⁴ is optionally branched C₁-C₆ alkyl or optionally branched C₁-C₆ alkenyl, optionally substituted with hydroxyl, halo (fluoro, chloro, bromo, iodo) thio, amino and cyano; and

R⁵ is optionally branched C₁-C₆ alkyl or optionally branched C₁-C₆ alkenyl.

4. (Currently Amended) The pharmaceutical composition of ~~any one of claims claim 1 and 2~~, wherein said cannabinoic quinone is a compound of formula (V):



wherein

X is an oxygen, nitrogen or sulfur atom;

p is zero when X is oxygen or sulfur, or p is 1 when X is nitrogen;

R¹ is H or C₁-C₆ alkyl;

R² designates a methylene group optionally substituted with up to two alkyl groups, wherein R² with the substituents comprises up to 5 carbon atoms;

R³ is optionally branched C₁-C₁₀ alkyl or optionally branched C₁-C₁₀ alkenyl, wherein said alkyl or alkenyl are optionally substituted with hydroxyl, alkoxy, halo (fluoro, chloro, bromo, iodo), thio, amino or cyano; and

R⁴ is optionally branched C₁-C₆ alkyl or optionally branched C₁-C₆ alkenyl, optionally substituted with hydroxyl, halo (fluoro, chloro, bromo, iodo) thio, amino and cyano.

5. (Currently Amended) The pharmaceutical composition of ~~any one of claims claim 1 to 3~~, wherein X is oxygen, R² is hydrogen, and R⁵ is 2-propyl or 2-propenyl.

6. (Currently Amended) The pharmaceutical composition of ~~any one of claims claim 1 to 2 and 4~~, wherein X is an oxygen atom forming a pyrane ring comprising two carbon atoms of the quinone ring to which said oxygen is attached and carbon atoms 3 and 4 of ring A, which pyrane ring is preferably 2,2-dimethyl substituted.

7. (Currently Amended) The pharmaceutical composition of ~~any one of claims claim 1 to 4~~, wherein R⁴ is methyl.

8. (Currently Amended) The pharmaceutical composition of ~~any one of claims claim 1 to 2~~, wherein said cannabinoic quinone is the compound 3S,4R-p-benzoquinone-3-hydroxy-2-p-mentha-(1,8)-dien-3-yl-5-pentyl (also designated HU-331).

9. (Currently Amended) The pharmaceutical composition of ~~any one of claims claim 1 to 2~~, wherein said cannabinoic quinone is the compound 6aR,10aR-1-H-dibenzo[b,d]pyran-1,4-(6H)-dione-6a β ,7,10,10a α -tetrahydro-6,6,9-trimethyl-3-pentyl (also designated HU-336).

10. (Currently Amended) The pharmaceutical composition of ~~any one of claims claim 1 to 2 and 4~~, wherein said cannabinoic quinone is the compound 1-H-dibenzo[b,d]pyran-1,4(6H)-dione-6,6,9-trimethyl-3-pentyl (also designated HU-345).

11. (Currently Amended) The pharmaceutical composition of ~~any one of claims claim 1 to 3~~, wherein said cannabinoic quinone is the compound 3S,4R-p-benzoquinone-3-hydroxy-2-[p-mentha-1-en-3-yl]-5-pentyl (also designated HU-395).

12.(Currently Amended) The pharmaceutical composition of ~~any one of claims claim 1 to 3~~, wherein said cannabinoic quinone is the compound 3S,4R-p-benzoquinone-3-hydroxy-2-[p-menthan-3-yl]-5-pentyl (also designated HU-396).

13.(Currently Amended) The pharmaceutical composition of ~~any one of the preceding claims claim 1~~, for the treatment of hyperproliferative disorders.

14.(Original) The pharmaceutical composition of claim 13, wherein said hyperproliferative disorder is a malignant or a non-malignant disorder.

15.(Original) The pharmaceutical composition of claim 13, wherein said hyperproliferative disorder is one of carcinoma, lymphoma, melanoma, glioblastoma and sarcoma.

16.(Original) The pharmaceutical composition of claim 14, wherein said non-malignant hyperproliferative disorder is psoriasis.

17.(Currently Amended) The pharmaceutical composition of ~~any one of the preceding claims claim 1~~, for intra-peritoneal (i.p.), subcutaneous (s.c.) or intratumor administration.

18.(Currently Amended) The pharmaceutical composition of ~~any one of claims claim 1 to 12~~, for the treatment of a disease or condition selected from inflammation and infections caused by bacteria, protozoa or fungus.

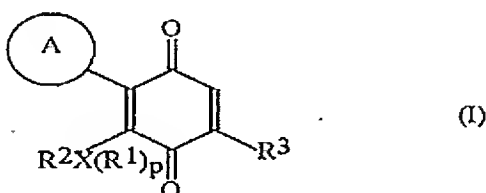
19.(Currently Amended) The pharmaceutical composition of ~~any one of claims claim 1 to 12~~, for the treatment of an autoimmune disease.

20. (Currently Amended) The pharmaceutical composition of ~~any one of the preceding claims~~ claim 1, optionally further comprising pharmaceutically acceptable additives, diluents and carriers.

21. (Original) The pharmaceutical composition of claim 20, wherein said carrier is a 1:1:18 (v/v) mixture of ethanol:Emulphor®:PBS.

22. (Currently Amended) The pharmaceutical composition of ~~any one of the preceding claims~~ claim 1, wherein said active agent comprises an optically active isomer or a racemic mixture of said cannabinoic quinone.

23. (Currently Amended) A method for the treatment of a hyperproliferative disorder, comprising administering to a subject in need of treatment a therapeutically effective amount of a cannabinoic quinone of formula I:



wherein,

ring A is 5-, 6-, or 7-membered alicyclic or aromatic ring optionally substituted with from 1 to 3 substituents selected independently from optionally branched C₁-C₈ alkyl, optionally branched C₁-C₈ alkenyl, hydroxy, alkoxy, halo (fluoro, chloro, bromo, iodo), thio, amino or cyano;

X is an oxygen, nitrogen or sulfur atom;

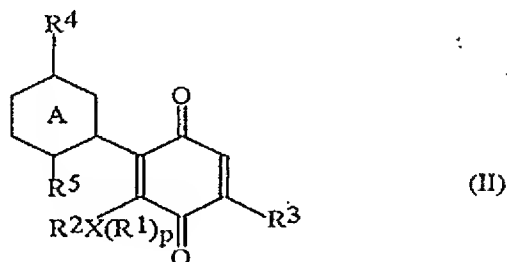
p is zero when X is oxygen or sulfur, or p is 1 when X is nitrogen;

R¹ is H or C₁-C₈ alkyl;

R^2 designates a substituent selected from H and C_1-C_5 alkyl, or R^2 designates an optionally branched C_1-C_5 alkylene connected to ring A forming a 6-membered heterocyclic ring comprising atom X, two carbon atoms of the quinone ring to which X is attached and carbon atoms 3 and 4 of ring A; and

R^3 is optionally branched C_1-C_{10} alkyl or optionally branched C_1-C_{10} alkenyl, wherein said alkyl or alkenyl are optionally substituted with hydroxyl, alkoxy, halo (fluoro, chloro, bromo, iodo), thio, amino or cyano; or of a pharmaceutical composition as defined in ~~any one of claims~~ claim 1 to 17 and 20 to 22.

24.(Original) The method of claim 23, wherein said cannabinoic quinone is a compound of formula (II):



wherein,

ring A is a cyclohexane, cyclohexene or benzene ring;

X is an oxygen, nitrogen or sulfur atom;

p is zero when X is oxygen or sulfur, or p is 1 when X is nitrogen;

R^1 is H or C_1-C_5 alkyl;

R^2 designates a substituent selected from H and C_1-C_5 alkyl, or R^2 designates an optionally branched C_1-C_5 alkylene connected to ring A forming a 6-membered heterocyclic ring comprising atom X, two carbon atoms of the quinone ring to which X is attached and carbon atoms 3 and 4 of ring A;

R³ is optionally branched C₁-C₁₀ alkyl or optionally branched C₁-C₁₀ alkenyl, wherein said alkyl or alkenyl are optionally substituted with hydroxyl, alkoxy, halo (fluoro, chloro, bromo, iodo), thio, amino or cyano;
R⁴ is optionally branched C₁-C₈ alkyl or optionally branched C₁-C₈ alkenyl, optionally substituted with hydroxyl, halo (fluoro, chloro, bromo, iodo) thio, amino and cyano; and
R⁵ is optionally branched C₁-C₈ alkyl or optionally branched C₁-C₈ alkenyl, or R⁵ is hydrogen when R² is alkylene.

25. (Currently Amended) The method of ~~any one of claims~~ claim 23-24, wherein said cannabinoic quinone is any one of HU-331, HU-336, HU-345, HU-395 and HU-396.

26. (Currently Amended) The method of treatment of ~~any one of claims~~ claim 23 ~~to 25~~, wherein said hyperproliferative disorder is a malignant or a non-malignant disorder.

27. (Currently Amended) The method of treatment of ~~any one of claims~~ claim 23 ~~to 25~~, wherein said hyperproliferative disorder is one of carcinoma, lymphoma, melanoma, glioblastoma and sarcoma.

28. (Original) The method of claim 27, wherein said cannabinoic quinone is one of HU-331, HU-395 and HU-396.

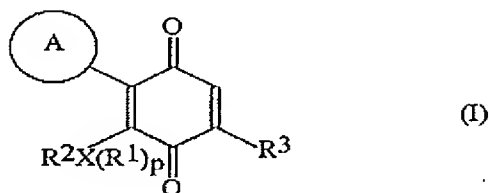
29. (Original) The method of claim 28, wherein said hyperproliferative disorder is one of colon cancer, lymphoma and breast cancer.

30. (Original) The method of claim 27, wherein said cannabinoic quinone is one of HU-336 and HU-345.

31. (Original) The method of claim 30, wherein said hyperproliferative disorder is one of prostate cancer and glioblastoma.

32. (Currently Amended) The method of ~~any one of claims~~ claim 23 to 31, wherein said cannabinoic quinone or composition comprising the same is administered via intraperitoneal, subcutaneous or intratumor route.

33. (Currently Amended) A method for the treatment of one of inflammatory, infectious and auto-immune conditions, comprising administering to a subject in need of such treatment a therapeutically effective amount of a cannabinoic quinone of general formula I:



wherein,

ring A is 5-, 6-, or 7-membered alicyclic or aromatic ring optionally substituted with from 1 to 3 substituents independently selected from optionally branched C₁-C₆ alkyl, optionally branched C₁-C₆ alkenyl, hydroxy, alkoxy, halo (fluoro, chloro, bromo, iodo), thio, amino or cyano;

X is an oxygen, nitrogen or sulfur atom;

p is zero when X is oxygen or sulfur, or p is 1 when X is nitrogen;

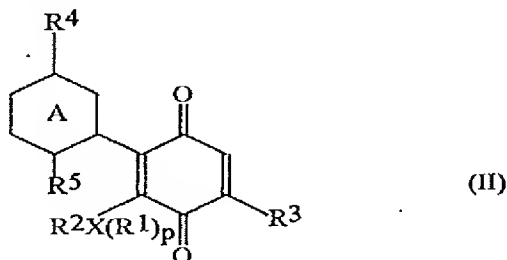
R¹ is H or C₁-C₆ alkyl;

R² designates a substituent selected from H and C₁-C₆ alkyl, or R² designates an optionally branched C₁-C₆ alkylene connected to ring A forming a 6-membered heterocyclic ring comprising atom X, two carbon atoms of the quinone ring to which X is attached and carbon atoms 3 and 4 of ring A; and

R³ is optionally branched C₁-C₁₀ alkyl or optionally branched C₁-C₁₀ alkenyl, wherein said alkyl or alkenyl are optionally substituted with hydroxyl, alkoxy, halo (fluoro, chloro, bromo, iodo), thio, amino or cyano; or

of a pharmaceutical composition as defined in ~~any one of claims claim 1 to 12 and 18 to 22.~~

34.(Original) The method of claim 33, wherein said cannabinoic quinone is a compound of formula (II):



wherein

ring A is a cyclohexane, cyclohexene or benzene ring;

X is an oxygen, nitrogen or sulfur atom;

p is zero when X is oxygen or sulfur, or p is 1 when X is nitrogen;

R¹ is H or C₁-C₆ alkyl;

R² designates a substituent selected from H and C₁-C₆ alkyl, or R² designates an optionally branched C₁-C₆ alkylene connected to ring A forming a 6-membered heterocyclic ring comprising atom X, two carbon atoms of the quinone ring to which X is attached and carbon atoms 3 and 4 of ring A;

R³ is optionally branched C₁-C₁₀ alkyl or optionally branched C₁-C₁₀ alkenyl, wherein said alkyl or alkenyl are optionally substituted with hydroxyl, alkoxy, halo (fluoro, chloro, bromo, iodo), thio, amino or cyano;

R⁴ is optionally branched C₁-C₆ alkyl or optionally branched C₁-C₆ alkenyl, optionally substituted with hydroxyl, halo (fluoro, chloro, bromo, iodo) thio, amino and cyano; and

R⁵ is optionally branched C₁-C₆ alkyl or optionally branched C₁-C₆ alkenyl, or R⁵ is hydrogen when R² is alkylene.

35. (Canceled)

36. (Canceled)

37. (Canceled)

38. (Canceled)

39. (Canceled)

40. (Canceled)

41. (Canceled)

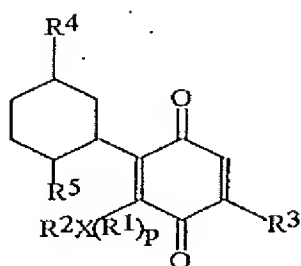
42. (Canceled)

43. (Canceled)

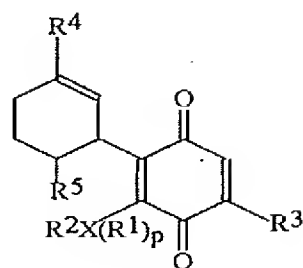
44. (Canceled)

45. (Canceled)

46. (Original) A compound of formula (III) or (IV):



(III)



(IV)

wherein

X is an oxygen, nitrogen or sulfur atom;

p is zero when X is oxygen or sulfur, or p is 1 when X is nitrogen;

R¹ is H or C₁-C₆ alkyl;

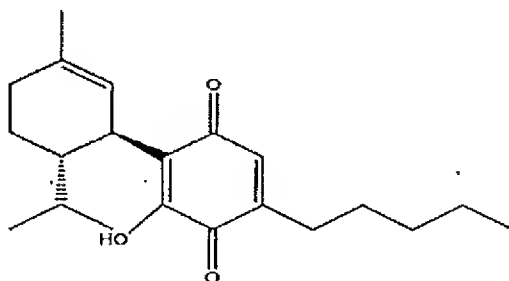
R² designates a substituent selected from H and C₁-C₆ alkyl;

R³ is optionally branched C₁-C₁₀ alkyl or optionally branched C₁-C₁₀ alkenyl, wherein said alkyl or alkenyl are optionally substituted with hydroxyl, alkoxy, halo (fluoro, chloro, bromo, iodo), thio, amino or cyano; and

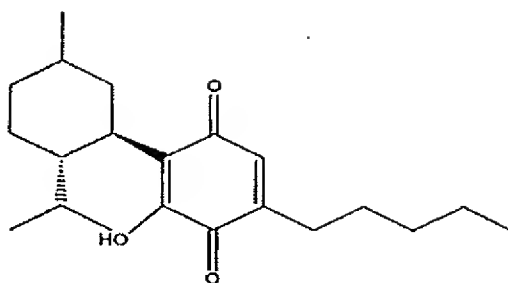
R⁴ is optionally branched C₁-C₆ alkyl or optionally branched C₁-C₆ alkenyl, optionally substituted with hydroxyl, halo (fluoro, chloro, bromo, iodo) thio, amino and cyano; and

R⁵ is optionally branched C₁-C₆ alkyl or optionally branched C₁-C₆ alkenyl.

47. (Original) The compound of claim 46, wherein said compound has one of the formulae:

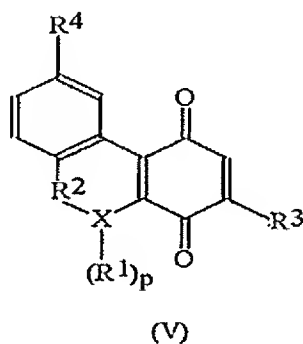


designated HU-395; or



designated HU-396.

48. (Original) A compound of formula (V):



wherein

X is an oxygen, nitrogen or sulfur atom;

p is zero when X is oxygen or sulfur, or p is 1 when X is nitrogen;

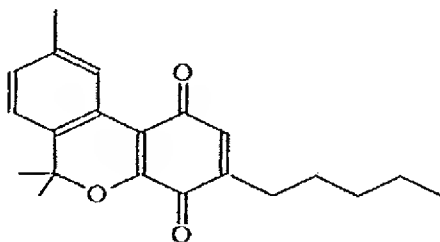
R¹ is H or C₁-C₈ alkyl;

R² designates a methylene group optionally substituted with up to two alkyl groups, wherein R² with the substituents comprises up to 5 carbon atoms;

R³ is optionally branched C₁-C₁₀ alkyl or optionally branched C₁-C₁₀ alkenyl, wherein said alkyl or alkenyl are optionally substituted with hydroxyl, alkoxy, halo (fluoro, chloro, bromo, iodo), thio, amino or cyano; and

R⁴ is optionally branched C₁-C₆ alkyl or optionally branched C₁-C₆ alkenyl, optionally substituted with hydroxyl, halo (fluoro, chloro, bromo, iodo) thio, amino and cyano.

49. (Original) The compound of claim 48, wherein said compound has the formula:



and is designated HU-345.

50. (Currently Amended) The optically active isomer and the racemic mixture of ~~each of the compounds~~ the compound defined in ~~claims 46-49~~ claim 46.

51. (New) The optically active isomer and the racemic mixture of the compound defined in claim 48.

52. (New) The optically active isomer and the racemic mixture of the compound defined in claim 49.